

ABSTRACT OF THE DISCLOSURE

5 The method of the invention provides the use of a replacement-type targeting construct to delete large fragments of genomic DNA by gene targeting. The replacement targeting construct, which may contain a selectable marker, is constructed to contain two regions of sequences which are homologous to the 5' and 3' flanking sequences of the targeted locus. After transfection of the targeting construct into the desired cell line, gene targeted-mediated
10 deletions are identified by selection and further characterized. The invention is useful in any situation where one would want to create a large genomic deletion. Examples of suitable loci include MHC Class I and II antigens and immunoglobulin genes, including, for example, variable and constant region of kappa, lambda, or heavy chains.